Proceedings of IMECE04
2004 ASME International Mechanical Engineering Congress and Exposition
November 13-20, 2004, Anaheim, California USA

IMECE2004-61569

INDUCTION OF MICRODAMAGE THROUGH APPLICATION OF ACOUSTIC ENERGY TO CORTICAL BONE

Andrea E. Tami
Dept. of Mechanical & Aerospace Engineering
Case Western Reserve University, Cleveland, OH
andrea.tami@case.edu

Melissa L. Knothe Tate
Depts. of Biomedical and Mechanical & Aerospace Engineering, Case Western Reserve University; Orthopaedic Research Center, CCF, Cleveland, OH

Jaime R. Streem
Orthopaedic Research Center
The Cleveland Clinic Foundation
Cleveland, OH

Ryan S. Comisford
Orthopaedic Research Center
The Cleveland Clinic Foundation
Cleveland, OH

Jared M. O'Leary
Orthopaedic Research Center
The Cleveland Clinic Foundation
Cleveland, OH

Stevan B. Streem
Urological Institute
The Cleveland Clinic Foundation, Cleveland, OH

Ulf Knothe
Orthopaedic Research Center
The Cleveland Clinic Foundation, Cleveland, OH
knotheu@ccf.org

ABSTRACT

Extracorporeal shock waves (ESW) are used routinely to break up kidney stones. Recently ESW has been implemented in the orthopaedic arena to treat heel spurs, although the mechanism underlying this therapeutic effect is not known. Acoustic energy has been shown to increase transport in bone. Furthermore, naturally occurring microdamage in bone has been implicated as a trigger for the onset of remodeling. We hypothesize that controlled application of ESW to bone tissue increases transport and stimulates bone turnover through production of low-level microdamage. The goal of this study was to identify the bandwidth and the application regime of acoustic energy to produce such damage. Transverse sections of sheep metacarpi (1 cm) were subjected to acoustic loading regimes of varying shock wave number and intensity. Thereafter, the blocks were bulk-stained with procion dye, embedded in PMMA, and sectioned into 100 mm slices for confocal microscopy and analysis. The blocks loaded with the highest energy regimes showed marked diffuse microdamage and microcracks, usually at sites of discontinuity along the periosteal edge. These results provide a first step in testing our hypothesis and ultimately may provide a basis for the exploitation of ESW to prevent osteopenia and/or osteoporosis.

Keywords: shockwaves, microdamage, bone remodeling.

INTRODUCTION

Women with hormone related, so-called type I osteoporosis, lose 3 to 4 percent of their bone mass per year. Although men and women with age related, so-called type II osteoporosis, lose somewhat less bone mass per year, the disease has a profound impact on quality of life in the aging individual. Disuse osteopenia associated with prolonged exposure to microgravity shows many parallels to osteoporosis on Earth. Astronauts lose bone mass at a rate of 0.5 to 2 percent of bone mass per month while living in microgravity, which amounts to a loss of 6 to 24 % of bone mass per year.

Human bone continually remodels itself as part of the normal repair and regeneration process. The fundamental mechanisms of remodeling are not well understood, but the process appears to be triggered through normal microdamage that occurs through physiological loading [1,2,5,6]. This microdamage may cause trauma to the cells, disrupt normal transport of cytokines, chemokines, growth factors and other signaling molecules. Each of these factors may, in turn, trigger a cascade of cellular events that result in osteoclastic resorption, and subsequent osteoblastic apposition.

In our current research program, we apply shock waves as an exogenous means to achieve the same effects of physiological loading on bone tissue, so that we may maintain and/or restore bone density on Earth and in space. This is in

stark contrast to urological applications where calculi are targeted for destruction and every effort is to avoid damage to the mineralized matrix of bone tissue [3,4]. Our approach is novel in that we apply extracorporeal shock waves with the intent to mimic naturally occurring microdamage that stimulates bone tissue to rebuild. Whereas a continued lack of physiological activity, including exposure to microgravity, will result in disuse osteopenia our working hypothesis is that prophylactic application of extracorporeal shock waves will cause microdamage in bone that will stimulate the remodeling, repair and renewal cascade.

METHODS

Extracorporeal shock waves were applied to 1 cm blocks from the ovine metacarpus using the Lithotriptor (Modulith® SLX). Waves were applied to the periosteal surface of the bone in the planar direction. The bone was maintained in Ringer's solution throughout each test. In order to define the appropriate regime for producing physiological looking microdamage, we applied one of six different regimes to each of the metacarpal blocks, in which wave number and peak pressures were varied, e.g. 500 or 1000 waves at 43, 76 or 100 MPa.

After application of the shock waves, the specimens were fixed in alcohol and bulk stained with procion red, a fluorescent dye that accumulates in voids of the tissue, *e.g.* within microcracks as well as blood vessels and porous regions. After staining, the specimens were embedded in plastic resin and sectioned with a diamond microtome for subsequent histomorphometric analysis. Specimens were imaged and high-resolution collages of the entire cross section were acquired using a computer-controlled epifluorescent microscope. This was necessary, because microdamage is only visible at very high resolution, but we still needed to know the location of all microdamage in each cross section. Each cross-section was imaged in fluorescent mode using a 10x objective. A total of 300-400 fields of view were acquired as images and concatenated into the single cross section.

Using a commercially available image analysis software (OpenLab), microdamage was identified and its extent was quantified within a semi-circle with 5mm radius in the corner of the cortex corresponding to the focal zone of the lithotriptor. The damage was normalized by dividing the sum of areas containing damage in the specific region by the total bone area of the same region. The total damaged area was averaged for three cross-sections from each block and a mean was calculated for the blocks subjected to the same treatment.

RESULTS

In all cases, damage was located almost exclusively in the cortex closer to the incoming shock waves (*i.e.* in the focal zone of the lithotriptor) and in close proximity to the periosteum. All 6 regimes of treatment showed more damage than the untreated control sample (Fig.1), and the location of areas of damage identified by two blinded investigators was closely matched.

Application of 1000 shocks produced more damage than did 500 shocks. For 500 shock waves, damage appeared to increase with increasing peak pressure; for 1000 shock waves the trend was inverted. Based on these data it is not yet possible to determine whether peak pressure or number of shock waves has a greater influence on energy dissipation and production of damage. The pores caused by fibrolamellar remodelling (Fig. 2) appear to influence energy dissipation through the tissue, most likely due to abrupt changes in impedance at their boundaries. Moreover, at the highest pressure level cavitation effects were evident, suggesting dissipation of energy through surface erosion instead of microcracks formation further in the cortex.

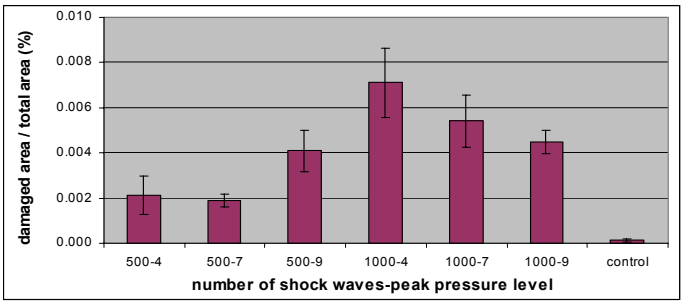

Figure 1. Ratio between selected areas with microdamage and total area of cortical bone in the focal zone of the lithotriptor.

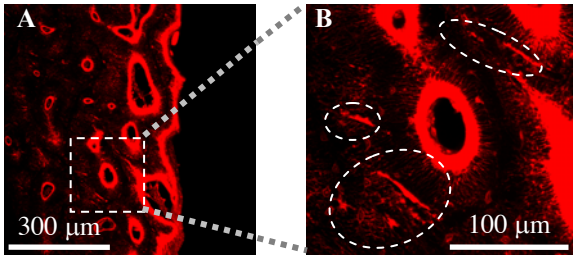

Figure 2. Images collected with the confocal microscope. Periosteal edge (A) and higher magnification showing overt microdamage (B).

DISCUSSION

Based on this preliminary study, application of high energy shock waves to cortical bone results in low level microdamage similar to that incurred naturally through physiologic activity. This study proves the feasibility of using acoustic energy in the form of extracorporeal shock waves to create microdamage and is a first step in testing our hypothesis that such exogenously induced microdamage can be exploited to induce remodeling in vivo, and, maintain bone tissue in a healthy state.

ACKNOWLEDGMENTS

The study was supported by a grant from NASA's John Glenn Bioscience and Engineering Consortium (JGBEC NCC3-1000).

REFERENCES

1. Bentolila V et al. 1998. Bone 23:275-281.
2. Mori S et al. 1993. Bone 14:103-109.
3. Ogden JA et al. 2001, Clin Orthop , 387:2-3.
4. Rajkumar P et al. 2002. Int J Clin Pract, 56:735-7.
5. Tami AE et al. 2002. J Bone Miner Res 17:2030-2037.
6. Verborgt O et al. MB 2000. J Bone Miner Res 15:60-67.